An Assessment of the Centers for Education and Research on Therapeutics (CERTs) Initiative

Submitted to:

The Agency for Healthcare Research and Quality

By:

The Washington Consulting Group

January 22, 2002

TABLE OF CONTENTS

1. INTRODUCTION

The Centers for Education and Research on Therapeutics (CERTs) is a Federal initiative designed to address an ongoing problem in health care research. The central objective of the CERTs initiative is to develop new and effective ways to improve the use of health care therapeutics throughout the nation's health care system. Therapeutics include drugs, biologics, and devices. The initiative combines support of basic health care research at research institutions (the centers) with concerted efforts to inform clinical practitioners and policy makers about the latest advances in therapeutics-related research.

The statutory authority for the CERTs is the Food and Drug Administration Modernization Act of 1997 (P.L. 105-115)**.** That legislation provided for a three-year demonstration program to conduct research on therapeutics and to publicize the research findings. The statute designated the Agency for Healthcare Research and Quality (then the Agency for Healthcare Policy and Research) to be the lead agency coordinating the CERTs effort. Since the program's inception, the Agency for Healthcare Research and Quality (AHRQ) has coordinated the program working in close consultation with representatives of the Food and Drug Administration (FDA).

The program design for the CERTs differs in some respects from most federally supported research programs. The core elements of the initiative, the research centers, are academic or non-profit health care research institutions with histories of research related to the use of therapeutics. For this initiative AHRQ chose not to provide oversight via a program officer managing each cooperative agreement on an individual basis. Instead AHRQ chose to establish a CERTs Steering Committee to perform many of the functions normally undertaken by program officers. In addition, the Steering Committee would provide strategic direction for the initiative as a whole and foster collaboration among the centers.

A CERTs Coordinating Center was established to enhance synergy among the various CERTs research centers. In addition, the Coordinating Center would identify and develop linkages with key government data sources. The Coordinating Center would also take a leading role in disseminating the results of CERTs research to the broader research community, to clinicians, and to health care policy makers.

In September 1999 the first four research centers were funded along with the Coordinating Center. Three more research centers were funded in 2000.

Objectives of the Project Assessment

This current study is intended to provide an assessment of the progress the CERTs has made to date in meeting its overall programmatic objectives. This study is not intended to critique the quality of the early individual research projects funded by CERTs grants. Rather, the purpose of this study is to assess the capability of the current CERTs

programmatic structure to adequately address all of the objectives stipulated in the authorizing legislation.

To perform this assessment the study team analyzed the following components of CERTs operations:

- **The organizational structure of the research centers funded to date.** To what extent do the centers currently address the objectives set for the CERTs? Should AHRQ consider providing more direction regarding the optimal "set up" or organizational structure for individual centers?

- **The role of the CERTs Steering Committee.** How successful has the Steering Committee been in supporting the unique aspects of the CERTs initiative? To date, what is the "added value" that the Steering Committee has brought to CERTs? Should the role of the Steering Committee be enhanced and/or modified?

- **The responsibilities of the Coordinating Center.** To what extent has the center enhanced the research capabilities of the various research centers? Has the Coordinating Center been able to increase the resources readily available to the researchers? What should be the short term "development plan" for the Coordinating Center that best addresses the CERTs' core objectives?

- **The status of CERTs' linkages.** One of the central objectives of CERTs was the establishment of effective linkages with public and private sector health care organizations. These linkages were to provide input (necessary resources and expertise for research) and assist in output (enhancing the impact of CERTs research in the broader research community and among policy makers.) Are the CERTs currently achieving this objective? Can this feature of the CERTs be significantly enhanced in the near term?

- **The role of the AHRQ program office.** Should AHRQ establish additional parameters to select and coordinate the activities of the centers? Does the current programmatic structure provide the right level of direction and prioritization for the operational components of the initiative?

Our goal in assessing each of these components was to identify realistic organizational enhancements.

Assessment Measures

The approach employed to assess the performance of each program component was based on the programmatic objectives set for the CERTs both in the authorizing legislation and in programmatic documentation developed by AHRQ. The goal was to assess how far the CERTS initiative has traveled towards the objectives set for it in the original legislation.

For each programmatic objective, measures of performance were developed that would indicate how much progress has been achieved to date. We obtained assessment data through a review of CERTs program documentation and research publications and through a series of interviews with key players in the CERTs initiative. The interviewees included senior researchers at the research centers, Coordinating Center staff, and members of the Steering Committee.

The core questions employed in our assessment included the following:

- **Uniqueness and significance of the research.** CERTs was designed to support research in an area that is clearly underrepresented in the existing research literature. A key measure of the CERTs assessment is the degree to which the initiative has been able to fund high quality research in the area of therapeutics. In short, has CERTs identified and funded research activities that meet the concerns identified in the authorizing legislation?

- **Expanding the resource capability of the therapeutics research community**. Has the CERTs developed a resource base (such as access to major Federal health care databases) that would assist therapeutics researchers both in current research and in the development of new research projects? Has the CERTs been able to develop an array of resources?

- **Development of operational linkages**. Have the research centers developed partnerships with public and private sector organizations? Have linkages provided non-federal funding, resources and expertise? Has the CERTs umbrella organization developed organizational linkages with Federal agencies (e.g., NIH) and other key players in therapeutics research? Has the research capacity of the CERTs expanded and were channels developed to enhance the impact of the CERTs on the research community, clinicians, and policy makers? What is the range of established linkages and are they substantive or merely pro forma?

- **Development of communication channels and initiative visibility**.Has the CERTs initiative put therapeutics research "on the map?" Has the CERTs identified and implemented effective communication strategies? Is the CERTs becoming a recognized authority in its area, i.e., the resource to which other Federal agencies and private sector organizations look to for guidance and research support?

- **Impact on research, practice, and policy.** The CERTs was not intended to be solely a research initiative. Did the research grants foster research on therapeutics while at the same time influencing clinical practice and health care policy? What impact has the CERTs had and what impact is it likely to have in the near term? Has the CERTs developed mechanisms that make future impact probable?

Where appropriate, the project team assessed the progress of each of the CERTs organizational components listed in the previous subsection. The progress achieved by the CERTS is documented in Sections 3 to 5. Recommendations for enhancements or logical “next steps” appear in Section 6.

2. PROJECT OVERVIEW

The main objective of the CERTs initiative is to fund and promote high quality research in the area of therapeutics. A brief summary of the range of research initiatives that the CERTs, through AHRQ, has funded in the initial phase of the program clearly indicates the success of the program in identifying appropriate and promising research initiatives within a very short timeframe.

Following is a summary of activities listed by research center.

The University of Pennsylvania

The University of Pennsylvania CERT, under the direction of Dr. Strom has mainly focused on increased risks associated with the use of drugs. Primary areas of research associated with this grant include the following:

- Evaluation of techniques to reduce the use of antibiotics for acute bronchitis in outpatient settings;
- Evaluation of the impact of antimicrobial formulary interventions at different hospitals on the resistance patterns of extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella species;
- Development of data simulations to expand the use of meta-analysis in the study of rare outcomes from antibiotics;
- Assessment of the effects of the use of tratraclycline in the treatment of acne focusing on antibiotic resistance patterns; and
- An epidemiological study of drug-resistant pneumococcal pneumonia.

At the Pennsylvania Center these research activities have been supplemented by a variety of educational initiatives intended to promote therapeutics research for medical students, medical researchers, and students in other health care fields.

Georgetown University (now directed from the University of Arizona)

Creating an infrastructure that will enable CERTs investigators to employ databases to identify harmful drug interactions has been the core objective at this CERT. An emphasis has been on serious drug interactions that pose the greatest risk for women. As problems are identified, the center develops communication tools to target patients most at risk, and health care providers most likely to be using the therapies investigated.

The initial research focused on problem of co-prescriptions. Long known to be an acute problem, the research data clearly indicate that adverse reactions can be life threatening. Research also confirmed that for drugs that block the potassium channel, life-threatening arrhythmia is more likely to occur in women. The center's researchers have already identified co-prescriptions that can significantly increase the risk of TdP ventricular arrhythmias in women. This research has already resulted in several information tools designed for health care professionals who may have to deal with such adverse reactions.

University of Alabama at Birmingham

Dr. Kenneth Saag is directing a CERT focused on musculoskeletal disorders (MSDs). The purpose of the CERT-funded research is to evaluate the effectiveness and safety of new MSD therapies and to provide guidance to the clinical community. Of particular importance is establishing the comparative effectiveness of well-known MSD treatments versus the large number of new products that have received FDA approval in recent years.

This CERT is developing educational and feedback mechanisms to improve the quality of MSD therapies offered in clinical settings. These provider-focused interventions will be based on analysis of the most recent research on combinations of therapies that appear to be most effective in alleviating the symptoms of specific types of MSD. Much of the pertinent data related to this analysis will be derived from MSD-related clinical trials conducted by the University of Alabama at Birmingham.

University of North Carolina at Chapel Hill

Dr. William Campbell is directing this CERTs initiative. This center coordinates a research and education agenda focusing on rational therapeutics for the pediatric population.

The center team is divided into three core research groups. The innovation group is addressing new drugs and devices for children. The best practices group is looking at development of effective strategies for delivering proven therapies. The monitoring and surveillance group is studying the need for improved surveillance on adverse events relating to the use of drugs and therapeutic devices in the pediatric age group.

This center has engaged in 16 selected and sequenced projects. The range of individual projects is wide. Innovation projects include development of evidence-based guidelines for assessing pediatric outcomes and assessment of the efficacy and toxicity of drugs given to HIV-infected pediatric patients. One of the initial best practices projects was an intervention designed to improve the clinical treatment of children with asthma. One of the monitoring/surveillance initiatives was a study of the use of psychotropic medications on children and adolescents in ambulatory care settings.

HMO Research Network

Dr. Richard Platt directs the research at this CERT. This CERT focuses on the analysis of patient data provided by member HMOs serving a population of 7.1 million people.

The core studies funded at this CERT include:

- Analysis of the frequency and reasons for antibiotic use in pediatrics;
- An assessment of the relationship between ACE inhibitor dosing in congestive heart failure and hospitalization; and

- Evaluation of the effect of changing drug co-payment requirements on diabetic patients' use of hypoglycemic agents

Duke University

Dr. Robert Califf directs the research center at Duke. The focus at the Duke Center is therapeutics in clinical medicine.

This CERT has been involved in ongoing demonstration projects designed to reduce errors of commission in the treatment of cardiovascular disease. Areas of concern include:

- Discovering and treating aspirin intolerant/allergic patients who have cardiovascular disease;
- Determining the most appropriate ways to initiate and maintain beta blocker therapy for patients with heart failure; and
- Determining the appropriate means to prescribe dofetilide treatment for patients with atrial fibrillation.

In addition to these research activities the Research Center at Duke has been working with the Food and Drug Administration (FDA) on surveillance programs for patients with cardiovascular disease. The areas of concern include:

- Transyocardial laser revascularization;
- New prosthetic valves; and
- Coronary stents.

Vanderbilt University

Dr. Wayne Ray directs research at the Vanderbilt Research Center. The Vanderbilt Center has undertaken several related studies focusing on encouraging rational pharmacotherapy in Medicaid managed care. The Medicaid population in Tennessee has been selected for the research focus because it has sub-populations that can be particularly vulnerable to sub-optimal pharmacotherapy. Such sub-populations include the developing fetus, young children, minorities, the chronically ill, the elderly, and individuals in nursing homes. In the Medicaid population all patients face severe income limitations.

Vanderbilt Center research includes:

- Conducting clinical pharmacologic and pharmacoepidemiologic studies including a post-marketing surveillance and pharmacoenonomic pilot study of the newly introduced Cox-2 NSAIDs;
- Developing intervention materials designed to modify sub-optimal provider or patient behavior; and

- Conducting a statistical assessment of the effects of policies on pharmacotherapy and clinical outcomes through a review of program and policy changes in the Tennessee Medicaid program.

3. ORGANIZATIONAL STRUCTURE

The CERTs initiative consists of a unique configuration of research centers, project directors, a Coordinating Center, and a Steering Committee. While the AHRQ assists the CERTs program, it does not direct, assume prime responsibility for, or play a dominant role in the CERTs. This responsibility rests solely with the individual centers and directors who work through the Coordinating Center, Steering Committee, and an array of highly active work groups. Each of these components has contributed to the progress and accomplishments of the CERTs program since it was established approximately two years ago.

Presented below are summaries of the self-assessment reports of the CERTs Coordinating Center and Steering Committee. Self-assessment data for the research centers is summarized in Section 4.

Coordinating Center Self-Assessment

A large majority of CERTs program directors, researchers, and their respective collaborators/partners, assert that the CERTS Coordinating Center has been highly effective in working with the Steering Committee, the individual research centers and their partners, AHRQ program officials, and FDA representatives. Project goals and objectives are clearly defined and articulated; research opportunities and the associated methodological and technical challenges are expeditiously brought to the attention of the research centers; and a host of pertinent and relevant CERTs information is reliably and frequently disseminated throughout both the CERTs program research centers and the national research community. Following are highlights of the Coordinating Center accomplishments:

- Held quarterly Steering Committee meetings. Several meetings focused on particular themes, such as patient safety. The Coordinating Center invited representatives from several organizations to discuss opportunities for collaboration on use of databases to address patient safety issues. In conjunction with another Steering Committee initiative, the Coordinating Center organized the Partners in Therapeutics Program to discuss partnerships to optimize the use of therapeutics. This meeting provided a forum for exploring potential collaborations that leverage individual effort.

- Organized several programs during the past year to increase awareness of AHRQ, the CERTs program and the centers' activities, as well create opportunity for public/private partnership.

- Enhanced synergy among the centers by coordinating efforts of all centers to respond collectively to the AHRQ RFA on patient safety research dissemination and education projects.

- Initiated a quarterly report summarizing the status of the research centers' education research. The report provides an overview of the CERTs projects for Steering Committee review and allows centers to learn about each other's projects and thereby facilitates collaboration among centers.

- In collaboration with the database workgroup, the Coordinating Center is developing a comprehensive catalog of data resources used in the CERTs program.

- Developed a process to streamline the Institutional Review Board (IRB) approval process relative to programs of research using specified data sets. The process was approved by the Duke IRB for Coordinating Center activities, and was shared with the centers so they could consider submitting to their IRBs for approval as well.

- Established a methods work group to facilitate potential collaborations among the centers on methodological projects. The following work groups continued to support discussions and activities in areas of common interest: public/private partnerships, publications, quality, and the Web.

- Enhanced dissemination activities through a focus on the development of an information kit and the expanded use of the CERTs Web site to inform practitioners, the public, the media, and others about the CERTs program and the work of the centers.

- Planning a series of expert workshops in collaboration with AHRQ, FDA, and PhRMA on assessing risk, communicating risk information, and managing risk to promote the optimal use of therapeutics.

Steering Committee Self-Assessment

CERTs project directors and associates praised the Steering Committee and its leadership as an integral part of the CERT program and a major catalyst and conduit for the exchange of information and ideas throughout the CERTs community. The Steering Committee is a public-private partnership with representatives from each of the CERTs centers, the Coordinating Center, AHRQ, FDA, and industry organizations. This collective body of expertise is credited with having helped the CERTs project obtain a high degree of national visibility and undertake a number of collaboration activities. It is generally believed that the Steering Committee, like the Coordinating Center, is doing an excellent job in fostering cooperation and collaboration between the different centers and between centers and the private sector. As we all know, cooperation is very difficult when various entities compete with one another. Of particular note was a special meeting sponsored by the Steering Committee in March 2001 in Washington, DC. This highly successful meeting provided a platform for the numerous participants to present research activities to a large group of attendees.

There was general agreement that that the management configuration of the CERTs, particularly the use of the Steering Committee, enabled it to make significant progress despite constraints. Research directors believe that the achievements are particularly significant given the unique requirements and parameters of the CERTs grant mechanism. Monetary shortfalls and the requirements for a multidisciplinary, yet focused, research agenda presented unusual challenges to the centers and their directorate. Despite these challenges, center leaders and associates consider the CERTs project a major success story.

Nearly all of the CERTs centers praised the genuine and very successful collaboration between the centers, Coordinating Center, and AHRQ. Many feel that the leadership is excellent and particularly high praise was given to the leadership at AHRQ. Synergy created by the CERTs program has, according to many, promoted research and dissemination of new therapeutics methods. Many also believe that the foundation has been laid for the CERTs program to eventually become a permanent and nationally recognized research institute for therapeutics education and dissemination.

There was general agreement that the Steering Committee was critical to progress CERTs has made to date. Important contributions of the Steering Committee include the following:

- Fostering a degree of collaboration and peer input that is seldom if ever achieved in areas of research dependent on the normal grant mechanism. The synergy achieved by the CERTs initiative is largely attributed to the Steering Committee, with the Coordinating Center serving as valued implementation tool.

- Serving as a highly visible mechanism that has developed important linkages with important external players including researchers, private industry, and other government agencies. The focus provided by the Steering Committee has ensured that such linkages benefit the entire initiative.

- Providing a mechanism that enables the CERTs to reach consensus-based decisions on critical issues, such as the role of private sector firms in establishing research agendas. The Steering Committee has maximized input to the decision process and assures that the research centers will pursue consistent policies.

Project Assessment

Based on data from key informant interviews and review of CERTs documentation, the project team made the following points regarding the operation of the CERTs Steering Committee and Coordinating Center:

- The technical support provided by the Coordinating Center needs to be enhanced. As stated above, our interviews indicated a high degree of satisfaction with the quality of the work performed by the Coordinating Center so far. However, there was also general agreement that the Coordinating Center needs to play a stronger role in gaining access to external resources and providing technical support to the various research centers. Significantly enhancing the technical capabilities of the center may not be feasible given current funding levels. This may be an area where the CERTs community may want to aggressively look for creative strategies to leverage external resources.

- The CERTs Steering Committee needs to set a more definitive research agenda for the entire program. It is quite clear that the initial phase of the CERTs has funded research initiatives of a high quality (see Section 4). However, there will soon be a need to set some strategic parameters for the type of research the CERTs supports. Such an initiative would likely be part gap analysis and part needs assessment. The Steering Committee is the obvious component of the CERTs to perform this function. The Steering Committee may want to consider broadening its representation if it takes on this task.

- The Steering Committee needs to work on broadening the base of the therapeutics research community since one of the ultimate objectives of the CERTs initiative is to increase the number of qualified researchers concentrating on therapeutics research. As of yet there is no targeted mechanism for the CERTs to address this objective. This should be a concern of the Steering Committee even if this initiative is delegated to another component of the CERTs.

- The Steering Committee needs to significantly enhance the level of active cooperation with other government health care agencies. There was general agreement that the level of input from other Federal agencies on the Steering Committee has not been sufficiently substantive. There was agreement that the CERTs needs greater proactive involvement of other health care agencies, both to obtain access to resources as well as to refine and expand the CERTs research agenda. The Steering Committee should set some specific strategic goals in this area.

- The Steering Committee needs to develop a mid- to long-term strategy for its growth as an institution. The tasks recommended above should logically be taken by the committee but this is realistic only if the committee has the funding, support, resources, and time commitment of its members. The recommended changes may be beyond the capacity of the committee's members, given its current composition. The Steering Committee will need to determine the extent to which it needs to become a true institution, and it ability to move seamlessly to a new generation of members without a diminution in effectiveness. If it decides not to "institutionalize," the committee will need to adopt a lead role in specifying how the tasks listed above will be addressed by the CERTs.

Recommendations directly relating to the assessments listed above appear in Section 6.

4. RESEARCH CENTERS

Achieving Research Objectives

The seven research centers were involved in about 100 different activities or projects as the second year came to a close. These projects ranged from planning to data collection to data analysis and presentation or publication. Web site design was and continues to be important for certain projects. Not all of the activities are new. Some of the projects that are now in the analysis and publication stage were selected as the first CERTs to be funded because of their research depth and expertise before the CERTs grants were awarded. Other projects only began once the grants were received.

Funding research on the clinical use of therapeutics

An obvious measure of a research initiative is its ability to identify and fund research activities that adequately address its objectives. On this score the CERTs has made major progress since its inception. Through its Request for Applications (RFA) process the CERTs initiative has been able to identify 7 research institutions engaged in projects that cover a range of topics related to the use of therapeutics. In its initial stage the CERTs has addressed a central objective of the initiative, i.e. funding research on the clinical use of therapeutics for a wide variety of sub-populations.

Working together to advance research objectives

The Coordinating Center and the individual centers joined forces to alert health care workers and the public to risk issues and to the inappropriate use and monitoring of drugs. CERTs proposed a series of workshops on the issue of risk; the first was held in spring 2001. The meeting, "Improving Communication of Drug Risk Information to Prevent Patient Injury," was held in Washington and included participants from government, academia, and industry. The meeting resulted in several promising initiatives.

A second activity of the combined CERTs has been the development of the Partnerships to Advance Therapeutics (PATHs), a project to cultivate public-private partnerships across the country. The first meeting of this group was held in Washington last spring and included participants from government agencies, caregivers, consumers, insurers, and others. As a result of this meeting the partnership group hopes to develop an Internet-based registry of educational and research projects.

Research Publication

The researchers at the centers have been extremely active in conducting research for major peer reviewed journals. Information on published articles and unpublished manuscripts as well as other outputs are shown in the table below:

Manuscript Status	*Number*	*Percent*
Total	95	100
Published	39	41
Publishing pending	15	16

Provisional acceptance	5	5
Submitted	15	16
Draft completed	8	8
Workshop proceedings	2	2
Book chapter: published	3	3
Book chapter: other	2	2
Conference proceedings	2	2
Other/status unknown	4	4

Data are summarized in a monthly report on the progress of each project undertaken by a CERTs center. Since most of the CERTs were funded in the fall of 1999, the centers have produced 82 journal manuscripts and 13 other types of publications or proceedings.

Forty-two (44 percent) of the manuscripts have been published in journals or as book chapters. Many were published in prestigious journals such as *JAMA* and *Pediatrics*. An additional 22 are at publication pending or provisionally accepted stage in various journals and books. Fifteen additional manuscripts have been submitted. Currently, eight more manuscripts have reached draft 1 completed status. The report does not make clear at what level the drafts will undergo CERTs review; this needs to be clarified.

The monthly reports may not accurately reflect the current status of CERTs-supported research. Some manuscripts reported to be in draft status show no progress over a number of months. Perhaps each center should be required to report the specific progress or reason for lack of progress when a manuscript's status has not changed in two or three months.

Journal articles produced under the CERTs grants have different goals, including academic research, clinical research and clinical research calling for health/physician interventions. A sample of journal articles is reviewed below and grouped by goal. One point of note is that many of the articles published using CERTs funding make no mention of CERTs or the source of the funding for the project described. The articles mentioned below describe research funded wholly or in part by the CERTs research centers. These articles are mentioned to underscore the progress the CERTs has made to date in supporting research that has direct application in clinical settings and for health care policy makers.

Academic research

Localio AR, Berlin JA, Ten Have TR, Kimmel SE. Adjustments for center in multicenter studies: an overview. *Annals of Internal Medicine*. 2001 Jul 17;135(2):112-23. Review. University of Pennsylvania School of Medicine.

Investigators often rely on multicenter or multigroup studies to demonstrate effectiveness and generalizability. Researchers need to be aware of possible confounding by patients grouped into centers.

Clinical research

Lark RK, Lester GE, Ontjes DA, Blackwood AD, Hollis BW, Hensler MM, Aris RM. Diminished and erratic absorption of ergocalciferol in adult cystic fibrosis patients. *American Journal of Clinical Nutrition*. 2001 Mar;73(3):602-6. University of North Carolina, Chapel Hill.

Researchers paired cystic fibrosis patients with matched controls and found that cystic fibrosis patients absorbed significantly less vitamin D. They theorize that this lack could be a contributing factor to low bone mineral density. Further study is needed.

Hennessy S, Strom. Statins and fracture risk. *Journal of the American Medical Association 2001* Apr 11;285(14):1888-9. University of Pennsylvania School of Medicine.

An editorial commenting on numerous studies that show conflicting results relating to statin use and fracture.

Clinical research calling for intervention

Rosebraugh CJ, Flockhart DA, Yasuda SU, Woosley RL. Visual hallucination and tremor induced by sertraline and oxycodone in a bone marrow transplant patient. *Journal of Clinical Pharmacology* 2001 Feb;41(2):224-7. Georgetown University Medical Center.

This article reports on serotonin syndrome probably caused by drug interactions. In complicated patients that are taking multiple medications, physicians should be aware of this possible interaction.

Kreiter SR, Schwartz RP, Kirkman HN Jr, Charlton PA, Calikoglu AS, Davenport ML. Nutritional Rickets in African American Breast-fed Infants, *Journal of Pediatrics*, 2000 Aug;137(2):153-7. Wake Forest University School of Medicine, University of North Carolina.

Childhood rickets is on the increase in this population. The review of babies treated in two North Carolina medical centers led to recommendation that all dark-skinned infants and children receive vitamin D supplements. Following these findings, the State of North Carolina is investigating providing vitamin D to infants.

Flockhart DA, Desta Z, Mahal SK. Selection of Drugs to Treat Gastro-Oesophageal Reflux Disease: The Role of Drug Interactions. *Clinical Pharmacokinet*, 2000 Oct;39(4):295-309. Georgetown University Medical Center.

This article summarizes interactions between antacids and other drugs used in the treatment of a Gastro-Oesophageal Reflux disease and medications prescribed for concurrent patient conditions.

Self-Assessment: Achieving Research Objectives

The project team conducted detailed interviews with representatives of each research center, with all members of the Steering Committee and with staff at the Coordinating Center. Many of the grantees felt that that their research objectives were being met and that their projects were widely known. However, many also felt that it was too soon to ascertain their effect on clinical practices and the research community.

Most grantees believed that the most effective method for disseminating information to practitioners is through publications in professional journals and through attendance and presentations at national and international professional meetings. All research centers have prepared manuscripts for publication.

Some were uncertain whether their centers had changed the research community but agreed that their work had influenced policy change and expanded the dialogue on these issues. For example, because of published information showing a link between a lack of vitamin D supplements and the development of rickets in breast-fed children, the Immunization Division of the North Carolina Department of Health and Human Services is considering making vitamin D available free to breastfeeding women throughout the State.

One research center has prepared and distributed to clinicians a brochure and patient videotape on treating congestive heart failure with beta-blockers. Another CERT has set up an on-line registry on arrhythmia and drug interactions, which has obtained international recognition and participation. CERTs also promotes heart disease projects that relate directly to Federal health programs such as the Healthy People initiative.

One respondent commented that there are now more ongoing discussions relative to risk management and therapeutic use. Another member of the CERTs network believed that CERTs is having an impact on research outside the network because the CERTs program is enhancing public dialogue and elevating conversations about the type of research and studies being conducted.

Self-Assessment: Research Partnerships and Networking

One goal of the CERTs was for the grantees to establish and/or improve research partnerships with the public and private sector in order to adequately address research objectives. The centers were mandated to seek useful, appropriate relations with private organizations to support and enhance education, research, and demonstration projects. In addition, a founding principle of CERTs was that grantees had to establish collaborative relationships with each other and the other CERT components. Grantees and other members of the network felt that CERTs succeeded in operating as a genuine collaboration between the centers, the Coordinating Center and AHRQ; and that the design lends itself to true synergy, far better than some had anticipated.
.

Over 100 partnerships have been formed with organizations including AHRQ, Research Triangle Institute, United States Pharmacopoeia, Columbus Children's Hospital, Quintiles, Inc., Glaxo Wellcome, Pfizer, United Health Group, the North Carolina Department of Health, Aetna, Arthritis Foundation, Upjohn, University of Pennsylvania Medical Center, NIH, EPIC, Department of Veterans Affairs, Infectious Diseases Society of America, Roche Laboratories, Agouron Pharmaceuticals, and DuPont. Some of the partnerships are new, but many are extensions of earlier relationships. Several private organizations were suggested in the assessment as partners for closer collaboration or as participants on the Steering Committee including the National Health Council, Family USA, and Women in Family.

There have been a number of successful partnerships to date between the grantees and Federal government agencies, especially with VA, FDA, and NIH. The FDA's member on the Steering Committee expressed enthusiasm about the projects undertaken in the FDA area. He expressed concern, however that the CERTs are undertaking too many individual projects. Possibly, there should be a vetting process where the Coordinating Center or Steering Committee would have a voice in whether an individual CERT should/could accept a particular project.

Because the CERTs now have a national reach and importance, the FDA member felt that the grantees should be more selective in projects they undertake. FDA was concerned also that the CERTs are not nationally representative, but based mainly on the East Coast. He further indicated that, in his opinion, the CERTs are academically based and not community based, although a few have community outreach efforts. He felt that the CERTs should expand the community outreach efforts.

Currently, NIH and FDA have members on the CERTs advisory committee. Some of the grantees felt that collaboration could be improved with more involvement and input on the part of NIH. Regarding important Federal players that are not currently involved in the CERTs initiative, more than one grantee stated that the Centers for Disease Control and Prevention, the VA, and the Centers for Medicare and Medicaid Services should become involved.

Partners may be a source of funding and some grantees could see institutionalization of these relationships in the future. Several grantees felt that it was very realistic to obtain some additional funding from partners, but at least one indicated that it takes ongoing effort and significant time to obtain money. One CERT mentioned that partnering with an outside organization did not necessarily lead to funding. In this case, the CERTs had to purchase data from the partner.

Most members of the CERTs network, including some Federal members of the advisory committee, believe that core support from the Federal government is vital and that individual projects should be expanded for the long-term. Most rated the possibility of building a CERTs network without Federal funding as very unlikely. They believe that if there is no core funding from the Federal government, there would be no CERTs or the CERTs might become biased if the major source of money was private.

Regarding cooperation between the different centers and between the centers and the private and public sectors, one respondent observed that "cooperation is very difficult when most of the time various entities are in competition, making cooperation naturally limited. This program eliminated that problem." An example of collaboration between CERTs is a project with Duke and the University of Alabama at Birmingham involving secondary prevention of fractures in nursing home patients. Other examples of collaboration between CERTs are a study on gout by University of Alabama at Birmingham and the University of Pennsylvania and a study of arrhythmia involving Duke and Georgetown.

The partnerships have provided access to data and shared expertise among partners. One grantee said the CERTs program has institutions talking seriously to each other and not producing random clinical studies. More than one grantee stated that they have access to databases that they would definitely not have had without the CERTs program. To date, there has been limited exchange of data between some CERTs, but it is believed that exchange will increase in the future. Although more databases are available, there were requests for access to additional databases, including Protocare Services, EpiMed, General Practice Research Database in the UK, and the Delaware Valley Case-Control Network. At least one CERT commented that they had hoped to have access to some FDA files not available to the public, but that no agreement has been reached. One respondent suggested expanding CERTs research by developing a national database of studies that enhance the medical community's knowledge of the best way to use new therapies.

Many of the research centers indicated that there are two areas that affect their ability to succeed—funding and the length of the grants. Some grantees stated that funding has been adequate because of the way the applications were structured. However, others have stated that funding is not adequate; funding is sufficient for pilot studies, but more is needed for patient studies. Additionally, more funds should be made available for extended training programs. There was a suggestion that too many individual projects may have been funded with the grants, which could be one of the causes of shortfalls in funding.

The length of the grants was another issue. It was mentioned that the time limits of the grants make it difficult to recruit. A suggestion was made to increase grants from 3 years to 5 years, which is apparently possibly in some agencies. Also, one of the grantees stated that the whole CERTs community should rewrite the RFA so that the ability to fund and refund CERTs will become broad and well balanced. One grantee felt that the time spent applying and reapplying for grants was onerous. In some cases, a great deal of time was spent applying for additional grants and no funds were awarded.

Project Assessment: Research Contributions and Networking

Based on document review and data from key informant interviews, the project team came to the following conclusions regarding the research component of the CERTs:

- Within a very short time frame the initial round of CERTs grants have funded a large number of research projects directly relevant to the objectives of the CERTs. As might be expected the initial grants have built on existing research initiatives and expertise. The funded research covers a wide range of therapeutic products and also focuses on topics relevant to several special populations such as children and low-income recipients of Medicaid services. To date the CERTs award process has been reactive, identifying and supporting high-quality research within the parameters of the research topic. At this point it is not clear if the funded research projects address all or most of the top priority health care policy concerns in the designated area. Prioritization has not been a major concern in the start-up phase of the CERTs.

- During the start-up phase the CERTs researchers have put only a modest emphasis on developing research strategies that access and employ the health care data resources of Federal agencies. The researchers have employed a standard research institution approach, focusing on research problems that are "doable" given the resources of a single research facility. As of now the CERTs has not been able to put in place a strategy to develop research projects that take advantage of Federal data resources. Such strategies might require collaboration between several funded centers.

- The research centers have developed partnerships with a wide variety of public, non-profit, and private sector organizations. Development of such partnerships was one of the key objectives of the original CERTs design, with a particular emphasis placed on the establishment of non-federal funding streams. The partnerships developed to date have been project specific. While centers have received valuable support for individual initiatives we believe it would be accurate to say that the CERTs, as an entity, has not developed stable partnership relationships. It is unclear if any such partnerships will be established in the near term, or if they would truly serve the core objectives of the CERTs. The CERTs management structure may need to address this directly in the next round of grant awards.

- The focus of the information dissemination at the research centers has been the traditional channels of the research community. A number of centers have begun to develop effective tools to disseminate CERTS-funded research findings. However, this aspect assuredly will need a higher priority in the next phase of the initiative, both at established and newly funded centers. The CERTs community should not only emphasize information dissemination, but also develop ways to develop a dialogue between the clinical/policy community and the CERTs researchers. Such a dialogue would likely enhance the ability of the CERTs to conduct research that can have general application and impact within comparatively short timeframes.

Recommendations directly relating to the assessment findings listed above appear in Section 6.

5. COMMUNICATION STRATEGIES

One of the unique features of the CERTs initiative is the emphasis placed on communication. The dual mission of CERTs is to conduct essential research and provide information about the most effective and safest therapies. When the initiative is fully implemented information from the CERTs will be channeled effectively to practitioners and policy makers. In short, it is intended that there be a "short bridge" between the research sponsored by CERTs and its impact on clinical practice and patient well being.

Presented immediately below is a summary of the information obtained about the communication strategies employed by the CERTs initiative to date. This is followed by an assessment of the CERTs communication strategies in light of the overall objectives of the initiative.

Self-Assessment of Communication Strategies

There was general agreement among key informants that the CERTs community has produced an impressive amount of publicly available data and information in a relatively short period of time. To some extent this represents the "backlog" of the expertise and research experience of the staff of the initial seven research centers. Still, the volume of material is impressive. However, there is less agreement as to whether the CERTs has yet developed a truly effective communication strategy to impact clinical practice and health care policy.

As of fall 2001, only two years since the funding of the first projects, CERTs-supported researchers have prepared almost 100 manuscripts. Most of these were prepared for established peer-reviewed journals such as the *Journal of the American Medical Association* and the *Journal of Pediatrics*. At this relatively early date a number of articles prepared by CERTs researchers are already being cited in the professional literature. CERTs researchers have also developed special presentations for professional workshops and conferences.

In the research community, the CERTs researchers are certainly making their presence felt both by the volume and the quality of their research. However, it is less clear that the CERTs as an entity is receiving the recognition that it should. However, the support provided by CERTs is not featured, if mentioned at all, in many of these research publications. Because of this, the CERTs name within the research community is probably not as prominent as it deserves to be.

In line with the general purpose of the CERTs, the centers have developed public information materials in addition to professional articles. These have included brochures, videotapes, educational modules, registries, toll-free helplines, Web sites, and CD-ROMs. One educational module was developed based on the results of a survey of medical school students and professors. The survey found low levels of information regarding drug interactions and misuse. The module is a one-hour Power-Point presentation on CD-ROM designed for training programs.

Similar modules are being planned at a number of the research centers. One of these will teach doctors how to measure QT intervals. Another will teach pharmacists to recognize drug interactions while another will instruct psychiatrists on the possible negative effects of some drug interactions. Another module for health care professionals on the appropriate use of QT-prolonging medications is being planned.
In addition, one research center is developing an interactive CD-ROM that will provide counseling to patients with arthritis.

Other public information materials produced to date include a brochure for clinical practitioners on treating congestive heart failure with beta blockers. A video tape for patients on the same topic has also been developed Another CERT has developed a Web site to provide educational programs on drug induced arrhythmia and one to provide information about drug interactions. The on-line registries on arrhythmia and drug interactions have already received international recognition and support. This has led to planning for a registry for Steven-Johnson Disease.

The brief summary above clearly demonstrates that the first 7 research centers funded have taken the public information objectives of the CERTS initiative seriously. Considerable resources have been devoted to development of public information materials. However, informants saw a clear need to develop a more efficient system to produce such materials, using synergistic resources that can be developed by the CERTs. In addition, there is a perceived need to determine the effectiveness of various communication strategies and to determine the areas where CERTs-produced materials can have the most impact.

Project Assessment of Communication Strategies

The project team made the following assessments based on a review of key informant data and CERTs documentation.

- Within the health care research community CERTs-supported researchers have made a significant contribution to the professional literature, particularly impressive given the short operational timeframe of the CERTs. However, most professional readers probably would not identify the research results with the CERTs. Greater emphasis should be placed on a standard policy for describing the nature and objectives of the CERTs in research articles based on CERTs-supported research.

- The volume and quality of professional literature based on CERTs-supported research is already having a demonstrated impact on the professional community. Findings from CERTs-supported research are already being cited in the professional literature. However, it is unclear if the researcher contacts usually accompanying such citations (e.g., one-on-one conversations or discussions at professional meetings) are being utilized to strengthen the CERTs. Our data review could not confirm if such professional contacts are

being aggressively tapped to broaden the base of senior researchers who might have an interest in conducting the type of research supported by the CERTs.

- To date, the CERTs community has not developed a reliable communication channel that can provide criteria for targeting CERTs research funds. The senior CERTs researchers certainly have information on areas where valuable research can be conducted. How can this core information base be expanded? What external information sources can be tapped to identify critical areas of concern in therapeutics research? Ideally, such information should be channeled through the Steering Committee. Our data indicates that the external representatives on the Steering Committee have not seen this as their role. The CERTs needs to identify the communication channel(s) that can provide this type of information on a consistent basis.

- In order to achieve its communication-related objectives, the CERTs will need to increase the level of internal resources devoted to communications. If the CERTs is eventually to have its intended impact on clinical practice and policy it will need to communicate effectively. This will require specialized expertise. An important organizational issue will be the division of labor in this area between the Coordinating Center and the various research centers. Can the Coordinating Center develop materials targeted to narrow population groups (e.g., clinical specialists?) Should the research centers be required to devote more resources to communication activities? This issue should be addressed in the near term.

- To date the CERTs has not been able to establish effective communication channels with the organizations and agencies that can have the most immediate impact on clinical practice. In the program design there is intended to be a "short-bridge" between CERTs-supported research and the delivery of health care services. The CERTs will need to determine the organizations and agencies that should be targeted and the most effective means to reach them. Such targeted organizations would likely include State and local public health agencies, residency programs, and the professional associations of clinical specialists. Not only should targeted organizations and agencies be identified, but proven and effective means of communicating with these entities also need to be identified. In addition, the CERTs community needs to determine if establishing such channels should be primarily a CERTs responsibility or could be more effectively performed in partnership with other Federal agencies.

- As of yet the CERTs has not explored the possibility of developing partnerships with other Federal agencies that have well-developed information systems. Given the limited resources of the CERTs this is an avenue that should be explored. By becoming a partner in existing information networks the CERTs would also help promote interest in therapeutics-related research in the wider professional community.

- The CERTs needs to consider ways to develop a synergy in communication strategies based on partnerships developed at the research center level. Many of these partnerships have the capability of providing communication resources. It needs to be determined if these resources can be utilized effectively for the entire initiative.

- To date, the CERTs has not placed a priority on developing materials for the general public. This does not appear to have been a core objective of the initiative. However, this is an area the CERTs may want to explore in its next phase. Many of the research concerns of the CERTs have direct relevance to the behavior patterns of individuals (e.g., drug interactions). Developing partnerships that produce public information materials may be an appropriate and highly effective means of impacting the quality of health care delivery. Any initiative of this type would need to be implemented in a partnership directed by the coordinating bodies of the CERTs.

.

6. IMPLICATIONS

This section provides a summary of the general conclusions about current challenges for the CERTs based on the assessment conducted by the project team. Specific recommendations are provided where we believe the assessment data supports such recommendations. In other instances we have identified general issues that we believe the CERTs community needs to address, but without providing specific guidance. Hopefully, this section of the report can serve as a management tool for the AHRQ and the CERTs Steering Committee as they move into the next phase of the initiative.

The conclusions concerning the CERTs initiative are presented in three sections that relate to three core CERTs activities, namely research, partnerships, and communication.

Research Activities

Specific conclusions drawn about CERTs-supported research activities include the following:

- When awarding grants, the CERTs needs to give greater emphasis to the potential for the near-term impact of research strategies of applicants. Have applicants considered governmental and community partnerships that show potential for positive impacts on health care? Have applicants received input that suggests that proposed areas of research are areas of concern for specific components of the health care system? Does a proposed grantee have a strategy for moving from research to application? Such issues should be given strong consideration in weighing the relative merits of grant applications.

.

- The CERTs community should develop a mechanism that broadens both the institutional base and the research focus of the initiative. Are there obvious and significant gaps in the areas of research currently funded by the CERTs? This could include both specific therapeutics as well as sub-populations with acute needs. In addition, the CERTs needs a well-defined strategy to broaden the institutional base of therapeutics research and prevent the usual complaint that "the grant money always goes to the same people." Such a strategy could involve both elements of the grant award process as well as proactive promotion of therapeutics research at professional meetings

.

- Related to the issue discussed immediately above, the CERTs needs to enhance the access to major governmental health care databases for CERTs-supported researchers. Examples would include data from the National Health and Nutrition Examination Survey, the National Health Interview Survey, both from the National Center for Health Statistics, and the Behavioral Risk Factor Surveillance Survey conducted by the Centers for Disease Control and Prevention (CDC). Such access would obviously broaden the range of research initiatives undertaken by CERTs researchers and possibly enhance the power of research findings. In addition, such access could be promoted in

grant application documentation, hopefully getting the attention of those whom may not otherwise consider applying for CERTs grants.

- Given the likelihood that CERTs funding will remain modest in the near-term, the CERTs needs to develop a prioritization mechanism. Input for such a prioritization should be drawn from a wide network. This would include not only external researchers (e.g., FDA and NIH) but also health care officials (Federal, State, local) and policy makers. The Steering Committee could hold structured expert meetings to obtain this type of input. This type of input would be helpful in developing selection criteria for the next round of CERTs awards.

.

- CERTs researchers should be strongly encouraged to involve clinical practitioners in their research designs. Such involvement will enhance the impact of CERTs-supported research. In addition, the involvement of clinicians should promote greater awareness of CERTs within the health care community thus fostering long-term partnerships.

.

- In the awarding of CERTS grants greater emphasis should be placed on the likelihood that research will lead directly to a tool or health care resource. Such emphasis should greatly enhance the short-term impact of CERTs supported research on clinical practice and health care policy.

Partnerships

Specific conclusions drawn about the partnering component of the CERTs initiative include the following:

- An enhanced partnership/operational linkage involving the State public health systems could contribute significantly to the growth and long-term viability of the CERTs program. The CDC, because of its long history of working with the Association of State and Territorial Health Officers (ASTHO) could help establish a CERTs working relationship with State government agencies. ASTHO often uses its Public Health Training Network Broadcast to communicate public health issues to CDC, HRSA, the FDA, and other HHS agencies. The CERTs, with its affiliation with AHRQ, would seem to be a logical partner in this linkage.

- The CERTs should consider developing partnerships with public advocacy groups with an interest in therapeutics research. Examples of such groups are the National Health Council, Family USA and Women in Family. Partnering with such organizations could alert the CERTs network to emerging public concerns. In addition, these organizations could be extremely effective in transmitting the findings of the CERTs researchers to the general public,

particularly special populations (e.g., women in specific age cohorts, children, etc.)

- The CERTs needs to develop truly operational partnerships with Federal departments and agencies involved in health care research. As mentioned above these agencies can provide access to resources that can possibly draw new investigators into therapeutics research. In addition, many of these agencies have established linkages with State and local agencies and important non-profit players. The CERTs should attempt to make these partnerships truly operational and not simply advisory. The CERTs should designate some body, perhaps a sub-committee of the Steering Committee, to identify the Federal resources that would most significantly enhance the resource base of the CERTs. The Steering Committee could then develop a detailed action plan to engage representatives of those departments/agencies in the CERTs network.

- The CERTs should explore the possibility of networking the partnerships that have been established at the research center level. As mentioned above, the resources provided and the level of commitment from the various partnerships has varied widely. The CERTs should identify the most promising partnerships that could synergistically benefit the entire CERTs research community. Identifying key research partners should assist in the development of more ambitious research projects and promote synergistic cooperation between the various research centers.

Communication Strategies

Specific conclusions about the communication aspect of the CERTS initiative include the following:

- The CERTs needs a mechanism to develop effective communication channels with public health agencies, particularly at the State and local levels. Effective contacts who have detailed knowledge of CERTs' products and objectives can provide input regarding important areas of research focus and can provide a means through which major CERTs research findings can have an impact on clinical practice and policy. To develop such channels the CERTs, through AHRQ, may want to develop close ties with other agencies. The Centers for Disease Control and Prevention would appear to be the leading candidate for such a role (see section on partnerships above).

.

- The CERTs should develop a detailed, long-term communication strategy. Such a strategy should include identification of key target audiences and the most effective ways to reach those audiences. Particular attention should be given to identification of communication vehicles that are most effective (e.g., whether a single Web site effectively serves all target audiences.) Developing such a strategy will probably require the support of an organization with

expertise in social marketing. Given funding restrictions this is another area where the CERTs may want to develop a partnership relationship.

- As an immediate goal, the CERTs should attempt to provide additional professional editorial resources through the Coordinating Center. While the researchers at the various centers have considerable experience in developing materials that meet the professional requirements of peer-reviewed journals, the CERTs would benefit from enhanced editorial resources that can generate materials oriented to non-specialist readers. A good start has been made but the CERTs obviously needs additional resources in this area if it is to effectively reach key target audiences and the general public.

- CERTs should make more use of existing public relations resources to reach its various publics. AHRQ resources can be tapped for this purpose. CERTs could consider holding press briefings before and after workshops or conferences. CERTs could also consider preparing press releases that would coincide with journal publications.

- The CERTs should assess its role in the design and implementation of public affairs campaigns (as opposed to the more targeted communication efforts mentioned above.) Most probably such an initiative would need one or more partner organizations. An effective campaign of this type could raise the level of public awareness regarding therapeutics issues and perhaps generate the type of ongoing industry support that was anticipated in the original authorizing legislation.

For more information

For more information on CERTs and this evaluation, please contact:
Judi Consalvo
Program Analyst
Agency for Healthcare Research and Quality
Center for Outcomes and Effectiveness Research
6010 Executive Blvd - Suite 300
Rockville, MD 20852
Tel: 301-594-0602
FAX: 301-594-3211
jconsalvo@ahrq.gov